Abstracts

Minisymposium 1

Pesticides

M1.1 NEUROLOGICAL SYMPTOMS AND PAST USE OF PESTICIDES

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Introduction: It has been proposed that repeated low level exposure to organophosphates, particularly in sheep dips, can cause a syndrome of ''chronic organophosphate induced neurological disease'' (COPIND), comprising various specified neurological symptoms. To explore this hypothesis, we analysed data from a survey of men aged 25–69 years in three rural areas.
Methods: Subjects (n = 34 486) were sent a postal questionnaire about various aspects of work and health, including: lifetime history of work with different categories of pesticide; the extent to which they had been bothered during the past seven days by each of five non-neurological somatic symptoms (summarised by a ''somatising tendency'' score); and experience of seven COPIND symptoms in the past month. The association of COPIND symptoms with potential risk factors was examined by modified Cox regression.
Results: Questionnaires were returned by 10 765 men (31%), including 9844 who provided full information on the seven COPIND symptoms. These symptoms tended to cluster within individuals, but the clustering was more marked among the 6109 men who had never worked with any pesticides (observed/expected with 4+ symptoms = 98) than in the 1913 who had worked with sheep dip (observed/expected = 48). Report of 4+ COPIND symptoms was strongly associated with somatising tendency (PR 21.1, 95% CI 14.4 to 30.9, for men in the highest category of somatisation), and after allowance for this, it was more common in past users of sheep dip than in those who had never worked with pesticides (PR 1.4, 95% CI 1.0 to 2.0). Within the group who had worked with sheep dip, risk was highest in those who had used sheep dip on 50+ days (PR 1.4, 95% CI 0.6 to 3.0 in comparison with <10 days), but there was no association with handling concentrate.
Conclusions: COPIND symptoms do not constitute a syndrome specific to work with organophosphates or sheep dip. They occur with marginally higher frequency in past users of sheep dip, and a toxic mechanism for this excess cannot be ruled out. However, their strong association with somatising tendency, and the fact that within men who have dipped sheep, their prevalence is not clearly associated with indices of higher exposure, suggests that they may often be psychologically mediated.

M1.2 PLASMA ORGANOCHLORINE PESTICIDES LEVEL AND RISK OF MAJOR LYMPHOMA SUBTYPES

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Introduction: Several reports of an increase in lymphoma risk associated with increased blood levels of persistent organochlorine (OC) pesticides corroborate earlier findings of an increase in risk of leukemia and lymphoma among farmers. We explored the hypothesis in a subset of cases and controls who participated in the European multicentre case control study on the etiology of lymphoma (EPILYMPH).
Methods: We measured the concentration of 17 OC pesticides, including hexachlorobenzene, four lindane isomers (α-,β-,γ-, and δ-hexachlorocyclohexane, two chlordane species (heptachlor and oxychlordane), four cyclodiene insecticides (Aldrin, Dieldrin, Endrin, and Mirex), and six DDT isomers, in a plasma sample of 671 subjects (325 lymphoma cases and 338 controls) from four European countries participating to the EPILYMPH study. Risk of lymphoma and its major subtypes by increasing plasma level of each individual OC pesticide was calculated using unconditional logistic regression.
Results: An increased risk of lymphoma was associated with a heptachlor plasma level above 47.1 ppb (OR 5.9, 95% CI 1.3 to 27.3). *o,p*-DDE showed a significant upward trend in risk of lymphoma. The association was stronger for follicular lymphoma and chronic lymphatic leukaemia (CLL). CLL risk associated with the highest quartile of *o,p*-DDE plasma concentration was 6.3-fold (95% CI 1.1 to 27.5). Among lindane isomers, only α-hexachlorocyclohexane (α-HCH) showed elevated risks, with a sevenfold excess risk in the highest quartile (95% CI 1.6 to 30.1) and a significant upward trend in risk only for CLL. p,p′-DDT isomers, cyclodiene insecticides and hexachlorobenzene (HCB) did not show an association.
Conclusion: We showed an association between increased plasma levels of heptachlor, α-hexachlorocyclohexane, and *o,p*-DDE, but not other DDT isomers and derivatives, nor hexachlorobenzene, with an increasing risk of lymphoma, and particularly CLL.

M1.3 EXPOSURE TO PESTICIDES AND IMMUNOLOGICAL EFFECTS IN CORN FARMERS IN IOWA

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Introduction: Farmers have an increased risk of non-Hodgkin's lymphoma (NHL) when compared with the general population. Altered immune function may be an indicator of increased potential for the development of immunologically based diseases such as NHL. The aim of this study was to investigate selected immunological markers in corn farmers with current exposure to pesticides.
Methods: Thirty corn farmers and 10 agricultural extension workers (controls) were followed for one growing season. The farmers completed daily diaries on pesticide use, farming activities, application methods, other exposures, and personal protective equipment during the planting season, followed by weekly diaries during the remainder of the season. Blood and urine samples were collected at six time points during the study period (before, during, and after planting; before and after harvest; off season). Biomarkers of exposure to selected non-persistent pesticides and/or their metabolites were quantified in urine. Immune status was investigated by measurement of lymphocyte subsets and activation markers, circulating cytokines, and immunoglobulins, and by performing lymphoproliferation assays to mitogen and recall antigens in vitro.
Results: On average, farmers (n = 30) were applying pesticides for 98 hours (range 23–227) between planting and harvest, with most applications taking place between April and July. Atrazine, glyphosate, 2,4-D, and chlorpyrifos were the most frequently used pesticides. If used, these pesticides were on average applied for 37, 45, 18, and 11 hours, respectively during the season. Baseline information on available cell counts and activation markers indicates an overall healthy population as values are generally within the normal range and most did not differ between farmers and controls, except for natural killer cells (p = 0.04), which were found to be lower in farmers than controls. T cell activation markers (CD-69 and CD-25) tended to be lower in farmers than controls and were statistically significant for CD4 (p = 0.07) and CD8 cells (p = 0.02) for CD69 and CD25, respectively.
Conclusions: There is considerable variation in pesticide use, both between farmers and within farmers throughout the growing season, which will provide the necessary exposure contrast to evaluate potential effects of pesticides on the immune system. At baseline, some differences in natural killer cell counts and early T cell activation markers were observed between farmers and controls, however, further analyses linking specific exposures to effects are still needed.

M1.4 PESTICIDE EXPOSURE AND NEUROBEHAVIORAL IMPAIRMENT: RESULTS OF THE 4 YEAR FOLLOW UP OF THE PHYTONER STUDY

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Introduction: Even if the neurological toxicity of certain pesticides, and especially insecticides, is well known, few studies have dealt with neurological effects of moderate but repeated exposure to pesticides. The aim of the PHYTONER cohort, initiated in France in 1997–98, is to assess cognitive effects of long term exposure to pesticides in vineworkers. At baseline, the risk of scoring a low performance on the tests was higher in pesticide exposed subjects. We present here results at the 4 year follow up.
Methods: PHYTONER is a cohort of 929 workers affiliated with the MSA (French Health and Welfare department for farmers) aged 40–55 years in 1995. Neuropsychological tests were administered by psychologists at the worker's home at baseline and at the 4 year follow up. Occupational histories were collected for all subjects on specific questionnaires, and workers were defined as non-exposed, directly exposed, or indirectly exposed to pesticides according to detailed tasks they perfomed. In the absence of a normative reference value, the performance threshold was the 25th percentile for the distribution of the scores and the 75th percentile for the distribution of times. We ran multivariate logistic regression adjusted on sex, age, level of education, depression, and alcohol consumption.
Results: 625 workers were interviewed at the 4 year follow up (67.3% of baseline workers) and 119 of them were non-exposed, 336 were directly exposed, and 159 were indirectly exposed. Non-respondants were slightly younger (51.5 *v* 50.1 years) and less educated but comparable in sex, nationality, smoking, alcohol consumption, and distribution of exposure. The risk of scoring low was higher in exposed workers at most of the tests. For instance, the risk of scoring low at the Benton test (compared with non-exposed) was 6.02 (1.71–21.13) for directly exposed (*v* 2.90 (1.53–5.48) at baseline) and 5.49 (1.56–19.35) for indirectly exposed (*v* 2.28 (1.21–4.30) at baseline).
Conclusion: Our results confirmed the association between pesticide exposure and cognitive impairment that was found at baseline, and some associations were found stronger at the 4 year follow up. Further analysis will be presented on the evolution of the scores between the two steps of the study.

M1.5 AGRICULTURAL ACTIVITIES AND PESTICIDE EXPOSURE: ELABORATION OF A MATRIX FOR USE IN EPIDEMIOLOGICAL STUDIES

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Introduction: To date, most epidemiological studies on long term effects of pesticides have relied on crude classifications of exposure (for example, farmers yes/no). One of the difficulties in pesticide exposure assessment is the diversity of active ingredients (over 900 different chemicals marketed in more than 9000 different products), and the lack of records of which pesticides were used by individuals. As a same farmer may use as many as several dozen different active ingredients in a single year, a reconstitution of the products used in entire professional careers which drew only on the memory of individuals could not be exhaustive and would contain distortion. This is why we propose to elaborate an historical matrix to provide probabilities, frequencies, and intensities of use of active ingredients in various French agricultural settings.
Methods: The first step consists in gathering six complementary sources of information: (i) agricultural recommendations by the Plant Health Protection body, (ii) treatment calendars provided by farmers, (iii) information from ACTA* on products marketed, (iv) information on registrations and withdrawals from the Agriculture Ministry, (v) information from professionnal associations of farmers, (vi) data from the industry (panel from the UIPP†). The second step consists in compiling and comparing the sources in order to define probablities, intensities, and frequencies of use for each active ingredient. The third step is the validation of the matrix by experts in each agricultural setting.
Results: We will present results of the first step of the matrix as the following sources have already been compiled in vineyards, fruit growing, and crops: recommendations by the Plant Health Protection body, treatment calendars, information from ACTA, and the panel from UIPP. We will also present crosses of these sources and preliminary assessment of the probability, frequency, and intensity of use of some selected active ingredients.
Conclusion: The elaboration of a matrix for exposure assessment in agriculture should provide useful information in epidemiological studies on long term effects of pesticides.

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M1.6 ACUTE PESTICIDE POISONING AMONG SMALL FARMERS IN BOLIVIA

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Introduction: The consequences of pesticide use are of concern in Bolivia as a result of increasing use. Known dangers are intoxications in humans and environmental pollution, which have been reported from studies in Bolivia during the last decades. To asses the magnitude and reasons for poisonings the actual study was undertaken as part of the PLAGBOL project, a development project financed by DANIDA.
Methods: A cross sectional study was realised with interviews and serum cholinesterase activity tests (ChE) of 201 volunteering small farmers, mean age 36 years (range 15–79), from 48 villages with a population of approximately 10 000 in the Andes region of La Paz county. Of these subgroups of male farmers using pesticides were included in an analysis of (1) the influence of spraying prevalence, (2) toxicity of pesticides used, (3) the use of personal protective devices, and (4) personal hygiene on (a) serum cholinesterase activity (n=170) and (b) symptoms after spraying past month (n=114). The data were analysed with linear and logistic regression analysis in STATA 8.0.
Results: The most toxic pesticides, mainly organophosphates, were used by a majority of the farmers. Common symptoms of acute occupational poisonings were experienced by 69% of the farmers over a spraying season, while 92% of the deadly intoxications were the result of suicidal attempt as reported by the farmers and found when revising the hospital journals. Significant different levels of ChE and odds ratios for having experienced symptoms after spraying were seen among groups of farmers with different pesticide exposure levels. BMI and knowledge of how to handle pesticides were shown to have influence on ChE, whereas smoking, the use of gloves, hygienic measures, and knowledge of how to handle pesticides where shown to have influence on symptoms.
Conclusion: Acute intoxications is a common problem in Bolivia related to pesticides use. The reason for this serious situation is a lack of effective control with import and sale of pesticides, aggressive marketing from pesticide companies and salesmen, poor knowledge of dangers, and improper handling among farmers and the population as a whole—issues which need to be addressed before this situation will improve.